REMARKS/ARGUMENTS

It is believed that the statement "Claims 2-14 are pending", appearing at the top of page 2 of the Office Action, is a clerical error. Accordingly, Applicant respectfully requests that the record be amended to show that claims 1-14 are pending or alternatively, that the Examiner clarify why claims 2-14 are pending as stated.

Objection under 37 CFR 1.75(c)

The Examiner has objected to claims 11 to 14 as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant respectfully submits that these claims have a proper dependent form in view of new claim 23 and arguments presented below traversing the 35 USC §102(e) rejection of claim 2.

Rejection under 35 USC §112

Claims 9 and 10 have been rejected on the basis of a lack of antecedent for the limitation "the concentration of HO-1 mRNA". This limitation has been replaced with "the concentration of HO-1 *encoding nucleotide sequence*" which finds an antecedent basis in claims 3 and 4 from which each of claims 9 and 10 depends, respectively. Two new claims 21 and 22 have been added which depend from claims 9 and 10, respectively, which further define the HO-1 encoding nucleotide sequence as "mRNA".

Rejection under 35 USC §102(e)

The Examiner has applied U.S. Patent No. 5,888,982 (issued March 30, 1999) by Perrella *et al.*, alleging that the subject matter of claims 1 and 2 is anticipated by this reference. According to the Examiner, the Perrella *et al.* reference discloses a HO-1 specific antibody linked to a detectable label and a HO-1 promoter sequence linked to a reporter gene, each of which is alleged to be a "means for determining" HO-1 protein or nucleotide sequence concentrations. In addition, the Examiner has cited *re Haller* as the authority in U.S. case law for establishing that printed matter for using a known product does not lend patentable distinction to a claimed invention.

Claim 1 has been cancelled and a new claim 23 added.

MPEP §2131 provides that:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The **identical invention** must be shown in as complete detail as contained in the ... claim." [Emphasis added.] *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim.

Contrary to the Examiner's statement that Perrella *et al.* anticipates claims 1 and 2, instructions are not disclosed in the reference for using a HO-1 protein or a HO-1 encoding nucleotide sequence as a biological marker in a manner that can be correlated with a prediction, diagnosis or prognostication of a dementing disease.

Moreover, referring to the Examiner's statement that "printed matter", i.e. instructions, for using a known product does not lend patentable distinction to a claimed invention, Applicant respectfully disagrees. If, as in the present case, the "printed matter" conveys a novel method for obtaining a desired result and the method is essential for operation of the components of the package, then the printed matter must be considered. Indeed, *In re Miller*, 418 F.2d 1392, 64 USPQ 46 (CCPA 1969) the court held that:

> The fact that printed matter by itself is not patentable subject matter, because non-statutory, is no reason for ignoring it when the claim is directed to a combination.

In the present invention, the instructions convey meaningful information for using the components of the commercial package in a manner that can be correlated with a prediction, diagnosis or prognostication of the dementing disease. Accordingly, differences between the claimed invention and the prior art cannot be ignored merely because those differences reside in the content of the printed matter.

There are numerous claims of issued U.S. patents directed to kits containing instructions which define method steps essential for the operation of the product and therefore lend patentable distinction to an invention, e.g. U.S. Patent No. 6,534,322. Therefore, Applicant respectfully submits that rejection of the claims on this basis is improper.

MPEP §2121.01 also provides that:

> "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an **'enabling disclosure'** ... ." *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). [Emphasis added.] A reference contains an enabling disclosure if the public was in possession of the claimed invention before the date of the invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

Perrella *et al.* discloses methods for preventing sepsis-associated hypotension in a mammal, including an *in vivo* diagnostic assay for identifying a mammal at risk of developing sepsis. The reference further describes that the underlying pathological basis of sepsis-associated hypotension is associated with *increased levels* of HO-1 along with a concomitant increase in HO-1-generated carbon monoxide. Increased levels in carbon monoxide in turn contributes to the reduction of vascular tone and hence, hypotension. As such, the methods disclosed by Perrella *et al.* rely on the discovery that *elevated* levels of the HO-1 in the vascular tissue of the

patient compared to a normal control is an indication that the patient may be at risk of developing or suffering from sepsis-associated hypotension. Consistent with this discovery are disclosed methods for preventing sepsis-associated hypotension by selectively inhibiting HO-1 expression or HO-1 enzymatic activity.

In contrast, the claimed invention focuses on the evaluation of HO-1 as a systemic biological indicator of a dementing disease at various stages of development which is predicated on distinctly different biochemical and physiological findings compared to sepsis-associated hypotension. One study does not beget the other. As such, Applicant submits that the reference relied on by the Examiner does not provide an enabling disclosure sufficient to arrive at the claimed invention.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection under 35 USC §103

The Examiner has also rejected claims 1 to 10 as obvious also in view of the Perrella *et al.* for similar reasons given above and further stating that although not expressly taught by the reference, the operating conditions for the claimed commercial package are well within the purview of a skilled artisan. Applicant respectfully disagrees.

In order to establish a *prima facie* case of obviousness, a rejection must satisfy the following three criteria:

1. There must be some suggestion, teaching or motivation to modify the reference or combine the references on which the rejection is based;

2. There must have been a reasonable expectation of success by the hypothetical person of ordinary skill in the art, at the time the invention was made, that the modification or combination would work to produce beneficial results; and

3. The prior art references(s) must teach or suggest all of the elements and limitations recited in the claims.

Applicant asserts that the first criteria is not met since the prior art reference does not suggest any desirability to combine the elements as claimed for assessing a dementing disease. Furthermore, the Examiner has not articulated explicit or factual findings on motivation or suggestion to combine the elements disclosed in the prior art to arrive at the Applicant's invention and thus support a 35 U.S.C. §103 ground of rejection. The evidence on which an obviousness rejection is based must be set forth in the Office Action. Conclusory statements of similarity or motivation, without any articulated rationale or evidentiary support, do not constitute sufficient factual findings.

In order for the second criteria to be met, a person of skill in the art should be able to arrive at a claimed invention through a minimum of experimentation. However, Perrella *et al.* disclose research findings and applications based on sepsis-associated hypotension which are completely unrelated to the field of Applicant's endeavor and irrelevant to the specific problems with which the inventor was concerned. On this basis, the findings of Perrella *et al.* can not be extrapolated to the findings and applications of present invention, i.e. assessing a dementing disease. By way of example, the methods for making a determination of sepsis-associated disclosed by Perrella *et al.* specifically rely on detecting *elevated* levels of HO-1 in the vascular tissue of a patient compared to a normal control. The correlation of elevated HO-1 levels to sepsis-associated hypotension has permitted a method for preventing the disease to be established through selective inhibition of HO-1 expression or enzymatic activity. In contrast, the applications of the present invention are predicated on a finding that *reduced* levels of HO-1 protein or HO-1 encoding nucleotide sequence levels compared to a normal control can be correlated to a dementing disease. As such, there is absolutely no suggestion in the teachings of Perrella *et al.*, or predictability in the art, that would provide direction for a skilled artisan to follow in order to arrive at the claimed invention with any reasonable expectation of success.

In addressing the third criteria, it is asserted that the prior art reference does not teach or suggest all of the elements and limitation recited in the claims. Moreover, as discussed above, Applicant disagrees that "printed matter" for using a known product does not lend patentable distinction to a claimed invention.

Again referring to *In re Miller*, 418 F.2d 1392, 64 USPQ 46 (CCPA 1969), the claims were rejected because they included limitations that were directed to printed matter. The court reversed the rejection and held that:

> The fact that printed matter by itself is not patentable subject matter, because non-statutory, is no reason for ignoring it when the claim is directed to a combination. Here there is a new and unobvious functional relationship between a measuring receptacle, volumetric indicia thereon indicating volume in a certain ration to actual volume, and legend indicating the ration, and in our judgement the appealed claims properly define this relationship.

Thus, the court held that if printed matter is functionally related to the other elements of the invention, the printed matter must be considered in determining whether the claimed invention is nonobvious in view of the prior art. "The Examiner cannot dissect a claim, excise the printed matter from it, and declare the remaining portion of the mutilated claim to be unpatentable. The claims must be read as a whole." (Emphasis added.)

Reconsideration and withdrawal of the rejection are respectfully requested.

In view of the forgoing, early favourable consideration of this application is earnestly solicited.

It is believed this responds to all of the Examiner's concerns, however if the Examiner has any further questions, he is invited to contact Joy Morrow at (613) 232-2486.

Respectfully submitted,

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